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New approach to relieving pain and distress during high-dose-rate intracavitary irradiation for cervical cancer

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ABSTRACT

BACKGROUND AND PURPOSE: To relieve the pain and distress experienced by women who undergo high-dose-rate intracavitary radiotherapy (HDR-ICRT) for cervical cancer and to improve the current status of gynecologic brachytherapy in Japan, a new intravenous anesthetic protocol involving the administration of a combination of propofol and ketamine was developed. The primary aim of this study is to investigate the efficacy and safety of this new anesthetic protocol during HDR-ICRT for cervical cancer.

METHODS AND MATERIALS: All the patients who were diagnosed with cervical cancer between December 2008 and February 2011, treated with three-channel brachytherapy and subjected to the new sedation protocol, were evaluated. A visual analog scale (VAS) was used to assess the pain during brachytherapy, and we collected VAS score at the next HDR-ICRT. Toxicities were graded using the Common Toxicity Criteria, version 3.

RESULTS: A total of 178 sessions of HDR-ICRT were delivered to 57 patients. The patients' median VAS pain score was 0 (range, 0–10). The most frequent side effect was Grade 1–2 nausea, which occurred in 33 sessions (34%). However, 13 of 14 patients received concurrent cisplatin chemotherapy. None of the patients experienced Grade 3 or 4 adverse events.

CONCLUSIONS: We have demonstrated that our new intravenous anesthetic protocol produces appropriate effects and can be performed by radiation oncologists who were required to finish training in basic life support and the cooperative system of emergency according to in-house guideline. © 2015 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Anesthesia; Intravenous; Cervical cancer; High-dose-rate intracavitary irradiation

Introduction

Intracavitary radiotherapy (ICRT) plays an important role in radiotherapy for uterine cervical cancer. ICRT exhibits a markedly enhanced curative potential in cases of carcinoma of the cervix (1).

However, for many women, the diagnosis and treatment of cervical cancer are physically and emotionally debilitating. Anxiety and discomfort are widely recognized side effects of gynecologic procedures, including simple gynecologic examinations, diagnostic tests, and treatment procedures (2). In the absence of appropriate sedation and analgesia, most patients will experience discomfort and strong pain during intracavitary brachytherapy. This can lead to problems during the procedure, such as inappropriate packing or applicator placement, which can result in an inadequate dose distribution, adverse effects on local control, and/or an increased risk of morbidities. Appropriate applicator placement must be achieved to obtain good local control, survival, and morbidity rates (3), but accurate insertion is difficult in patients who are experiencing discomfort. Thus, methods that facilitate the quick, adequate, and safe administration of anesthetic drugs, and hence, reduce the pain experienced by cervical cancer patients during brachytherapy are required. The American Brachytherapy Society recommends that conscious

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sedation should be used for high-dose-rate (HDR) ICRT insertions whenever possible (4).

Previous pattern of care studies unexpectedly found that in Japan many patients undergo HDR-ICRT applicator insertion without receiving any analgesic drugs (5, 6), and even when such drugs are administered, their effects are often inadequate. In the United States and Europe, most patients who undergo pelvic brachytherapy are placed under general anesthesia by anesthesiologists; thus, the co-operation of anesthesiologists is vital for such procedures (7). However, this might be hard to achieve in many Japanese facilities because of manpower shortages. Therefore, in Japan, radiation oncologists are usually required to perform certain anesthetic procedures by themselves.

Under these circumstances, to relieve the pain and distress experienced by women who undergo HDR-ICRT for cervical cancer and to improve the present status of gynecologic brachytherapy in Japan, a new intravenous anesthetic protocol involving the combined use of propofol and ketamine was developed in collaboration with a board-certificated anesthesiologist (N.N-T.). Propofol is a short-acting intravenous sedative, and ketamine is a dissociative anesthetic that has strong analgesic effects and exhibits rapid onset and recovery and a wide margin of safety. Ketamine and propofol have been successfully used in a variety of settings, including sedation for cosmetic and anorectal surgical procedures performed in office suites, pediatric hematology/oncology units, and emergency departments (7–10). Combination of propofol and ketamine was based on the opposing hemodynamic and respiratory effects of the two drugs (10), which were considered to enhance the utility of the combination; that is, to increase its safety and efficacy and allow lower doses of each drug to be used (which would reduce the risk of side effects). However, there have only been a few studies about sedation using ketamine and propofol during HDR-ICRT (2, 11, 12). The primary aim of this study is to investigate the efficacy and safety of this new intravenous anesthetic protocol during HDR intracavitary brachytherapy for cervical cancer.

Methods and materials

All the patients who were diagnosed with cervical cancer between December 2008 and February 2011, treated with three-channel brachytherapy using uterine tandem and ovoid applicators and subjected to the new sedation protocol, were evaluated. Radiation was delivered using a microSelectron device (Nucletron BV, Veenendal, The Netherlands) and an iridium-192 source that demonstrated nominal activity of 10 Ci. HDR brachytherapy dosimetric planning was performed in all patients using a semiorthogonal system with a simulation box. The PLATO system was used for computerized planning (Nucletron BV, Veenendal, The Netherlands). This protocol needed the drugs (propofol and ketamine), oxygen, patient monitor (electrocardiography, heart rate, blood pressure, pulse oxymetry, and respiratory rate), and patient-controlled analgesia pump (or syringe driver). Radiation oncologists and experienced nurses trained under anesthesiologists' supervision for the first 5 patients. In our institution, radiation oncologists and nurses were required to finish training in basic life support and the cooperative system of emergency. During procedures, the trained nurses monitored the patients' vital sign including respiratory and circulation systems. In the brachytherapy room, we prepared an emergency cart, including laryngoscope, bag valve mask, endotracheal tubes, suction machine, and resuscitation drugs.

The patients' vital signs and oxygen saturation were continuously monitored throughout the procedure by the radiation oncologists and trained nurses. Supplemental oxygen was delivered at a rate of 2 L/min via a nasal cannula to all patients during the procedure. First, we administered propofol intravenously using an i-Fusor patient-controlled analgesia pump (JMS, Tokyo, Japan) at an initial dose of 10 mg. This was then followed by a maintenance infusion, which was delivered at a dose rate of 2 mg/kg/min. About 20-mg demand boluses were limited to four per hour and subject to a 5 min lockout period. We also intravenously administered ketamine diluted in 100 mL normal saline at a dose of 1 mg/kg. When half of the ketamine had been administered, we made the patients adopt the lithotomy position. Then, when three-quarters of the ketamine had been administered, we started to insert the instruments and perform the procedure. After the irradiation, a bolus of propofol was administered, and then the instruments were removed. The nurses who assisted with the procedural sedation recorded the patients' vital signs before, during, and after the procedure.

Propofol is a nonopioid and sedative–hypnotic drug. Its duration of action is approximately 6 min (9,10). Its adverse effects include hypotension and respiratory depression. However, because of propofol's brief duration of action, such side effects generally disappear quickly and uneventfully. Propofol does not have any analgesic effects, and therefore, additional treatment with an analgesic might be necessary.

Ketamine has strong analgesic effects and displays rapid onset and recovery and a wide margin of safety. Unlike general anesthetics, ketamine supports the cardiovascular system and so does not depress ventilation (10).

Eastern Cooperative Oncology Group Performance Status and American Society of Anesthesiologists Physical Status Classification (Table 1) were evaluated retrospectively. Vital signs were assessed by monitoring blood pressure, heart rate, and oxygen saturation before, during, and after the brachytherapy procedure. We scored the patients' sedation levels on the Ramsay Sedation Scale by retrospectively reviewing their nursing records (Table 2) (13).

The pain experienced by the patients while they were under sedation was assessed using a questionnaire containing a visual analog scale (VAS). Toxicities were

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